

### REMARKS

The claims were subjected to a restriction requirement. The applicants elected Group IV and the compound of Example 78 as the species. The Examiner kindly expanded the breadth of Group IV. The claims are amended herein to conform with revised Group IV. Claims directed to non-elected compounds have been canceled. Claims 32-36, directed to methods of use, were withdrawn by the examiner. They are shown in the listing of claims as withdrawn, and have been amended so that they depend on the claims that are being examined. They should be rejoined with the compound claims now under examination once the compound claims been allowed.

#### Amended Claims

Claims 1-3 have been canceled, and Claim 3 has been rewritten as new Claim 37, which uses formula Ib to define the compounds.

Claim 37 is supported as follows:

- The definition of Z was taken from Claim 1.
- X was limited to -CONH-, as required by the restriction requirement.
- R<sup>2</sup> was limited to benzyl as required by the restriction requirement, and the substituent definitions on the benzyl were taken from Claim 24.
- R<sup>3</sup> was taken from Claim 1, but with the addition of H as an additional selection. This is supported by dependent Claims 26 and 27, which included H as a selection. Without this change, large numbers of the claimed compounds are outside the scope of Claim 1.
- R<sup>4</sup> was taken from Claim 1.
- R<sup>9</sup> and R<sup>10</sup> were both taken from Claim 1. Only the values of R<sup>9</sup> and R<sup>10</sup> that fit with the compounds that were actually made were used (H and alkyl).
- R<sup>11</sup> and R<sup>12</sup> were both defined as H, which conforms with many of the dependent structures and all of the examples.
- R<sup>5</sup> and R<sup>6</sup> were taken from Claim 30. As R<sup>5</sup> and R<sup>6</sup> did not include several of the compounds, additional definitions corresponding exactly to those specific substituent groups were added.
- The values of n and m that were claimed were defined in the restriction requirement: n = 0, 1, or 2, and m = 1 or 2. As there are examples in the

elected group of compounds or in non-elected groups of compound that include all of these values of n and m, these are adequately enabled.

Other dependent claims are self-explanatory. A new Claim 40 was added for the substituent group R<sup>5</sup> that originally did not include several of the examples. It is supported by the specific examples.

### Objections

The table defining some of the specific compounds (Example 68-70) has blank spaces, as pointed out by the examiner. These blank spaces are for R<sup>3</sup> and R<sup>4</sup>, which are attached to Z. Z is defined as C, N, or O, where it is attached to R<sup>3</sup> and R<sup>4</sup> if it is carbon, but only to R<sup>3</sup> if it is N, and has no attachments if it is O. The blank spaces in the table are for compounds in which Z is O or N.

### Rejections under 35 USC § 112, second paragraph

Claim 19 was canceled so that the rejection is moot.

Claim 31 was canceled and replaced with Claims 38 and 39, which claim the species that were alluded to in Claim 31.

### Rejections under 35 USC § 112, first paragraph

The examiner cites publications that suggest that the binding of synthetic compounds to the CCR2 receptor is very sensitive to the substitutions on the phenyl of the benzyl group R<sub>2</sub> in structurally similar compounds and on the length and structure of the specific linker group in structurally similar compounds.

First, with respect to the benzyl group, applicants wish to cite US2006-0116421 (Butora I), which was filed on the same date as the instant application and describes a class of compounds that have structural similarities to the compounds in the instant application. The compounds in the Butora I application are benzyl amides that are CCR2 antagonists. Note that the compounds that were selected as examples in the series of compounds in Butora I have a wide range of substitutions on the phenyl on the right side of the structure, as can be seen in Table 2 (pages 43-47) and also by reviewing the list of chemical structures in Claim 30. Compounds having a benzyl group which comprises a

phenyl group substituted with substituents other than two trifluoromethyl groups are clearly also active.

Similarly, US 2005-0261325 (Butora II) was also filed on the same date as the instant application. It also discloses CCR2 antagonists that are benzylamides, as are the compounds in the instant application. There are numerous examples in the Butora II application of active compounds that have substituents other than two CF<sub>3</sub> groups on the phenyl. These include Examples 18-4 to 18-8 (pages 49-50), 34-37 (pages 62-63), 39, 40, 42, 45 (pages 63-64), and 93-97 (pages 85-86).

These provide a reasonable expectation that a broader range of compounds than just a bis-trifluoromethylphenyl compound will have activity in the compounds claimed in the current application. The claims have been amended so that they are directed to a smaller group of substituted benzyl groups than the original claims. It is believed that these meet the standards of enablement.

With respect to the linker groups, there are only two linkers used in this application, which are -CH<sub>2</sub>CH<sub>2</sub>- (m=1) and -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>- (m=2). Most of the examples are directed to compounds in which m is 1, but there is at least one example in which m is 2 in a non-elected group of compounds (Ex. 4). Thus the claims are well enabled for m=1 and 2.

#### Summary

It is respectfully submitted that the claims are adequately enabled and are in condition for allowance. Such allowance is earnestly solicited.

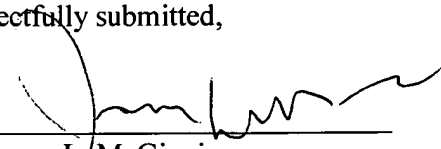
If the examiner needs to discuss any matter relating to this application, the examiner is invited to telephone the undersigned attorney at the number below.

A fee is not believed to be required with this timely response. If any fee is required, the fee may be charged to Merck Deposit Account No. 13-2755.

Please also take note that an Information Disclosure Statement is included with this response citing 4 patent applications that were filed on the same date as this application.

Respectfully submitted,

By



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